

## **REMARKS/ARGUMENTS**

### **Status of the Claims**

Upon entry of the present amendment, claims 74-75 and 78-109 are pending. Claim 74 is amended to incorporate the language of claims 76 and 77. Claims 76 and 77 are canceled.

### **Interview with the Examiner**

Applicants thank Examiner Alexander for graciously granting the telephonic interview with Applicant and Applicants' attorneys on October 12, 2005. The issues discussed during the interview are set forth in the Interview Summary. During the interview, Applicants proposed language for amending independent claim 74. Examiner Alexander indicated that the new claim language would be considered.

### **Rejection under 35 U.S.C. 102(e) over Köster**

The Examiner has rejected claims 74-109 under 35 U.S.C. 102(e) as allegedly anticipated by U.S. Patent No. 5,605,798 ("the '798 patent"). This rejection is respectfully traversed.

The '798 patent is only prior art with regard to subject matter that is entitled to a priority date prior to May 27, 1994

As an initial matter, Applicants respectfully assert that the '798 patent can only be considered prior art under 35 U.S.C. § 102(e) with regard to the subject matter disclosed therein that is entitled to a priority date *prior to* Applicants' priority date, May 27, 1994. The '798 patent was filed on March 17, 1995 and is a continuation-in-part application of U.S. Application No. 178,216, filed January 6, 1994, now U.S. Patent No. 5,547,835 ("the '835 patent"). The present application claims priority as a continuation application under 35 U.S.C. § 371 to

International Application No. PCT/US94/06064, filed on May 27, 1994, which precedes the March 17, 1995 filing date of the '798 patent.

The disclosure of the '798 patent that precedes the May 27, 1994 priority date of the present invention is found in the '835 patent, which again was filed on January 6, 1994. Therefore, Applicants respectfully assert that it is the disclosure of the '835 patent, and not the disclosure of the '798 patent, that is appropriate for discussion regarding the present rejection under Section 102(e).

The '835 patent does not disclose or suggest the claimed invention

As the Examiner well knows, proper anticipation requires that the cited reference teach or suggest each and every element of the claimed invention. M.P.E.P. § 2131.

The '835 does not disclose or suggest each and every element of the claimed inventions. The present claimed probes, methods and apparatus all require a moiety that binds to biotin (*e.g.*, streptavidin) immobilized by chemical bonding to a sample presenting surface on a mass spectrometry probe. The '835 patent does not disclose or suggest immobilizing a moiety that binds to biotin on a mass spectrometry probe.

Instead, the '835 patent discloses a method of sequencing DNA using mass spectrometry (*see*, Figure 1). The '835 patent discloses using Sanger DNA sequence methods well known in the art at the time of its January 6, 1994 filing date. The '835 patent discloses attaching a linking functionality ("L") at the 5' end of the dideoxy nucleotide terminated nucleic acid sequences. The linking functionality (L) can bind to a suitable binding functionality (L') on a solid support to form a temporary linkage to condition the terminated nucleic acid sequences (*i.e.*, nested Sanger DNA fragments) for mass spectrometry analysis (*see*, column 11, line 52 through column 12, line 10).

The '835 patent discloses two ways to condition nested DNA fragments for mass spectrometry analysis. They are depicted in Figure 1. In the first way, shown in Figure 1, the nested Sanger DNA fragments are temporarily linked to a solid support (that is *not* a mass

spectrometry probe) through a L-L' interaction, subjected to a wash/purification step, cleaved from the solid support, and then subjected to mass spectrometry. This is depicted by the downwardly pointing arrows in the center of Figure 1, and described, for example at column 11, line 52 through column 12, line 10. In the second way, also shown in Figure 1, certain kinds of L-L' temporary linkages can be subject directly for mass spectrometry analysis. This is indicated by the arrow by-passing the washing and cleavage steps at the bottom of Figure 1.

The '835 patent discloses only one example of a temporary linkage that can be cleaved under conditions of mass spectrometry—a photocleavable bond. This assertion is supported in at least two different locations in the '835 patent. First, at column 12, lines 4-10, the '835 patent discloses:

“In addition to the examples given in which the nested fragments are coupled covalently to the solid support, washed, and cleaved off the support for mass spectrometric analysis, the temporary linkage can be such that it is cleaved under the conditions of mass spectrometry, i.e., a photocleavable bond such as a charge transfer complex or a stable organic radical.”

Second, at column 13, lines 15-30, the '835 patent organizes the L-L' temporary linkages into three categories according to methods for their cleavage: enzymatic, chemical or physical. A biotin/streptavidin interaction is one of the several exemplified L-L' temporary linkages that are chemically cleavable, for example, by subjecting to mildly acidic conditions (*see*, column 13, lines 18-25). Chemically cleavable bonds are cleaved prior to mass spectrometry analysis. By contrast, a physically cleavable bond, or a bond that can be cleaved under conditions of mass spectrometry, is again equated with a photocleavable bond (*see*, column 13, lines 29-31). Exemplified photocleavable bonds contemplated in the '835 patent, including charge transfer complexes or stable organic radicals, are depicted in Figures 20 and 21. They are distinct from a biotin/streptavidin interaction.

In no instance does the '835 patent disclose or suggest immobilizing by chemical bonding a biotin binding moiety (*e.g.*, streptavidin) on the sample presenting surface of a mass spectrometry probe, a required element of the claimed inventions.

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PATENT

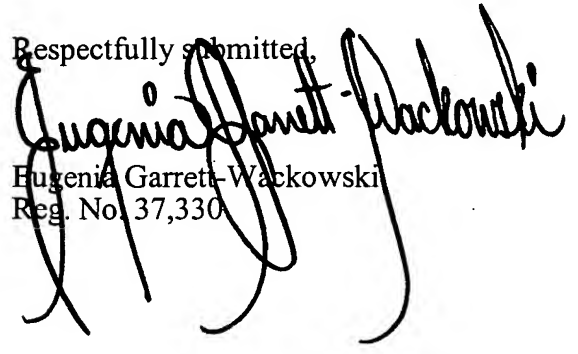
In view of the foregoing, it is clear that the disclosure of the '835 patent (which is the earlier filed disclosure of the '798 patent) does not teach or suggest each and every element of the claimed inventions. Therefore, the '835 patent does not anticipate the claimed probes, methods and apparatus. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

  
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